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10/540,247	06/05/2006	Michel De Waard	273623US0XPCT	6609

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EXAMINER	
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ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
12/11/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/540,247	DE WAARD ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *3,4,8-13 and 15-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-7,14 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/26/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I and the specie described in example 1 in the reply filed on 1/24/08 and further clarified on 8/11/08 as identifying the species as SEQ ID NO:14 is acknowledged.

Applicants state that the specie corresponds to claims 2,6-7. Since claim 6 depends from claims 1 and 5, claims 1 and 5 also read on the species. It is noted that applicant did not identify any mutations or labels. It is noted that claims 14,33 also read on the elected species.

As discussed below the elected species was found to be obvious based on the prior art. Any art that reads on non-elected species that was uncovered in the search for the elected species is cited herein.

Claims 3-4,8-13,15-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1/24/08 and further clarified on 8/11/08.

Claims 1-2,5-7,14,33 are under consideration.

Specification

The disclosure is objected to because of the following informalities:

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

In the instant case, applicants have not provided a section entitled 'Brief description of the drawings'. Further, it is noted that the specification makes reference to Figure 8c 9page 24 line 31), however there is no Figure 8c.
Appropriate correction is required.

It is noted that applicants state that they elect the specie described in Example 1. Example 1, specifically lines 34-35 refer to a rat beta 3 subunit whose cDNA corresponds to positions 98 to 1545 of the Genbank sequence M88755 (which was provided to applicant with the 3/19/08 correspondence). However, the genbank entry for M88755 is for the house mouse not the rat (see attached document). As such, there is a descrepancy as to whether or not the elected species

includes a beta subunit from a rat or from a house mouse. Further, entry M88755 has residues 1 to 879. Residues 98 to 1545 are referred to in example 1 (page 25 line 34). As such, the example is not consistent with the Genbank entry that is referred to.

Claim Objections

Claims 1,33 are objected to because of the following informalities:

Claim 1 recites 'at its NH2 or COON end'. It is noted that claim 2 recites 'COOH' and original claim 1 recited 'COOH'. Thus it appears that a typographical error has occurred and 'COON' should be 'COOH'.

Claim 1 recites 'BID domain' (see specification page 7 line 15) and 'AID domain' (see specification page 4 line 10-11). The abbreviations should be written out the first time that they are used in the claims.

Claim 33 is dependent on a withdrawn claim. Claim 33 recites 'any claim 28' which apparently should be 'claim 28'.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 14 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 14 recites that the peptide comprises at least 7 amino acids of the protein of claim 1. The protein of claim 1 includes the beta subunit and alpha1 subunit of naturally occurring proteins. The beta subunit of the naturally occurring protein reads on claim 14. The alpha1 subunit of the naturally occurring protein reads on claim 14. It is noted that the claim recites the 'junction'. However, there is no requirement that the peptide must contain elements on both sides of the junction. It is noted that claim 14 uses the open-ended language 'comprising' (see MPEP section 2111.03).

There is no indication that the peptides of the current invention have been isolated or removed from a naturally occurring environment. The claimed subject matter therefore reads on a product of nature.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation. It is noted that claim 14 does not require a BID domain.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2,5-7,14,33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claims refers to 'the BID domain'. The specification (page 7 lines 9-15 and page 4 lines 17-18) states that BID is the beta subunit interaction domain. On page 9 (line 14-15) it is stated that BID is as defined above. However, the metes and bounds of the

'interaction domain' are not clearly set forth. The term 'interaction domain' is not defined by the claim, the specification does not provide a standard for ascertaining an 'interaction domain', and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is noted that the specification does provide direction as to the metes and bounds of the AID by providing information on a conserved motif (page 4 lines 10-12 for example). However, identifying the AID does not lead one to the BID. It is noted that Figure 2, for example, does not provide precise information as to the metes and bounds of the BID. There is no specific direction provided as to how to delineate the beginning and end of the BID. Since the specification does not provide a standard for ascertaining an 'interaction domain' different approaches used to ascertain an 'interaction domain' would lead to more than one reasonable interpretation of the BID.

Claim 1 and dependent claims refer to the 'I-II loop'. Claim 2 recites that the protein consists of a specific element and the I-II loop. The specification (page 5 line 32-39) states that the I-II loop of the alpha1 subunit corresponds to positions 367 to 487 with reference to the Ca(v)alpha(2.1) subunit. Figure 1 lists residues 360-488 under the term I-II loop. Figure 1 also lists the heading Ca(v)alpha(2.1). As such, the metes and bounds of the term 'I-II loop' are unclear. In other words, applicants own specification provides more than one reasonable interpretation of 'I-II loop'. In particular, it is unclear if residue 361 is part of the I-II loop. The term 'I-II loop' is not defined by the claim, the specification does not provide a standard for ascertaining a 'I-II loop', and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In particular, it us unclear how to ascertain the I-II loop of subunits

other than Ca(v)alpha(2.1). There is no specific direction provided as to how to delineate the beginning and end of the I-II loop.

Claim 33 refers to 'chimeric protein' and 'the nonhuman transgenic mammals'. There is insufficient antecedent basis for 'nonhuman transgenic mammals' in the claim. Further, it is unclear if 'chimeric protein' is meant to refer to the chimeric protein of claim 1 or to a different chimeric protein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 14 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/05419 (abstract only as cited previously 11/28/07).

WO 01/05419 (abstract) teach a peptide of sequence QQLEEDLKGYLDWITQAE and is described as a peptide that imitates the alpha1 sub-unit interaction domain. It is noted that the instant application teach that the AID domain has the motif QQ-E--L-GY--WI---E (page 4 line 12). Thus the peptide of WO 01/05419 meets the structural limitations of the AID domain and as such is a component of the junction between a beta subunit and an alpha1 subunit. It is noted that the claim recites the 'junction'. However, there is no requirement that the peptide must contain elements on both sides of the junction. It is noted that claim 14 uses the open-ended language 'comprising' (see MPEP section 2111.03).

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation. It is noted that claim 14 does not require a BID domain.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2,5-7,14,33 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Waard et al (JBC v270 May 19 1995 pages 12056-12064 as cited in IDS) and Dolly et al (WO 03/035690).

De Waard teach the properties of the alpha1-beta anchoring site in voltage-dependent Ca2+ channels (title). De Waard teach that voltage-dependent calcium channels allow for the activation of numerous processes (page 12056 first paragraph). De Waard teach a goal of a

detailed analysis of the alpha1-beta interaction aimed at resolving the structural determinant involved in the specificity of subunit recognition (page 12057 first paragraph). De Waard discuss the identification of the molecular targets of channel regulators such as G proteins and teach that an in vitro method for the study of the alpha1-beta interaction will be useful for screening of drugs (page 12063 last paragraph).

De Waard specifically teach (page 12056 right hand column first complete paragraph) that Ca2+ channel subunits are separated into distinct classes including alpha1 (classes S,A,B,C,D, and E) and beta (beta1, beta2, beta3, and beta4). De Waard teach (page 12057 left hand column last paragraph) the use of various subunits from a variety of organisms including rats and rabbits. De Waard teach the importance of the cytoplasmic loop between domains I and II of the alpha1 subunit (abstract). De Waard specifically teach a diagram of the alpha1-beta interaction site (Figure 1). De Waard teach alpha interaction sites (AID) and beta interaction sites (BID) (Figure 1).

De Waard does not expressly teach a chimeric protein as in claim 1 of the instant invention.

Dolly teach about K+ channels, specifically expression, screening and therapeutic methods and molecules related thereto (page 1 lines 3-5, claim 22, abstract). Dolly teach fusion polypeptides that include the alpha subunit and beta subunit of the K+ channel (page 4 lines 4-9, claim 1, 35, abstract). Dolly teach that assembling the subunits allows for detailed biochemical analysis for use in drug screening (page 4 lines 12-15). Dolly teach fusion proteins with a beta subunit and an alpha subunit (page 17 lines 8-10). Dolly teach that intact fusion polypeptides

were expressed and assembled in significant quantities (page 10 lines 14-17). Dolly teach that it is preferred that the subunit polypeptide retain the relevant structural features that are present in the naturally occurring subunits (page 13 lines 21-22).

Since De Waard teach a goal of a detailed analysis of the alpha1-beta interaction aimed at resolving the structural determinant involved in the specificity of subunit recognition (page 12057 first paragraph) and discuss the identification of the molecular targets of channel regulators such as G proteins and teach that an in vitro method for the study of the alpha1-beta interaction will be useful for screening of drugs (page 12063 last paragraph) one would be motivated to analyze the alpha1-beta interaction and develop methods for the screening of drugs. Dolly also teach methods for screening (page 1 lines 3-5) and teach the methods for channel proteins. Although Dolly teach the methods for K+ channels, one of skill in the art would recognize that technique of forming fusion proteins would be applicable to Ca2+ channels and that methods of forming fusion proteins was recognized as part of the ordinary capabilities of one skilled in the art. It is noted that Dolly teach fusion polypeptides that include the alpha subunit and beta subunit of the K+ channel (page 4 lines 4-9, claim 1, 35). One would recognize that the Ca2+ channel also has alpha and beta subunits. Dolly teach that assembling the subunits allows for detailed biochemical analysis for use in drug screening (page 4 lines 12-15). One would recognize that such biochemical analysis for use in drug screening can be obtained for Ca2+ channels as well. Since Dolly teach that intact fusion polypeptides were expressed and assembled in significant quantities (page 10 lines 14-17) one would have a reasonable expectation of success.

Since Dolly teach that fusion polypeptides include the alpha subunit and beta subunit of the K+ channel (page 4 lines 4-9, claim 1, 35) one would be motivated to make fusion polypeptides of the alpha subunit and beta subunit of the Ca2+ channel. Since De Waard specifically teach (page 12056 right hand column first complete paragraph) that Ca2+ channel subunits are separated into distinct classes including alpha1 (classes S,A,B,C,D, and E) and beta (beta1, beta2, beta3, and beta4) one would be motivated to make fusion polypeptides using specific classes. It is noted that De Waard specifically teach alpha1 class A (AIDa of Figure 1) as well as beta3 (page 12057 left hand column, 3rd line from the bottom). Therefore one would be motivated to create an alpha1 class A-beta3 Ca2+ channel fusion protein (i.e. subunit alpha1 class A from a calcium channel fused to the subunit beta3 from a calcium channel) thus meeting the limitations of claims 1,5-7,14,33 of the instant invention. It is noted that such fusion would necessarily comprise a BID domain and AID domain as well as include a fusion at the NH2 or COOH end. It is noted that as claimed, claim 33 requires a 'fusion protein'. As discussed above, De Waard and Dolly obviate fusion proteins such as alpha1 class A-beta3 Ca2+ channel fusion protein. Further, it would be obvious to include such proteins in containers to form a kit. For example, Dolly teach that formulations can be stored in containers (page 49 line 19-20).

Since Dolly teach that it is preferred that the subunit polypeptide retain the relevant structural features that are present in the naturally occurring subunits (page 13 lines 21-22) one would use the teachings of De Waard to fuse the relevant portions of the subunits as well. Since De Waard teach the importance of the cytoplasmic loop between domains I and II of the alpha1 subunit (abstract, Figure 1) one would be motivated to create a fusion protein of the beta subunit and the I and II loop of the alpha1 subunit thus meeting the limitations of claim 2 of the instant

invention. Further, since De Waard teach (page 12057 left hand column last paragraph) the use of various subunits from a variety of organisms including rats and rabbits one would recognize that the rat I-II alpha1 loop or the rabbit I-II alpha1 loop could be used.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation. Claim 33 has been interpreted as referring to the chimeric protein of claim 1.

As noted above (see section 'specification' last paragraph) the identity of the elected species is unclear since example 1 and SEQ ID NO:14 do not seem to be in agreement. Since De Waard teach the importance of the cytoplasmic loop between domains I and II of the alpha1 subunit (abstract, Figure 1) one would be motivated to create a fusion protein of the beta subunit and the I and II loop of the alpha1 subunit thus meeting the limitations of claim 2 of the instant invention. It is noted that De Waard specifically teach the beta3 subunit (page 12057 left hand column, 3rd line from the bottom). Further, since De Waard teach (page 12057 left hand column last paragraph) the use of various subunits from a variety of organisms including rats and rabbits one would recognize that the rat I-II alpha1 loop or the rabbit I-II alpha1 loop could be used thus meeting the limitations of the elected species as currently interpreted.

In the instant case, the claims would have been obvious because the substitution of known elements (Ca2+ subunits) for other known elements (K+ subunits) would have yielded predictable results to one of ordinary skill in the art at the time of the invention. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention

as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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